# Case Report

# Dimenhydrinate: evidence for dependence and tolerance

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Dimenhydrinate is considered to be a reliable and safe nonprescription drug for which dependency has not been documented. Although tolerance to its sedative properties can develop,[1] this has never before been reported.

We present two patients in whom dependency and tolerance occurred — in one to striking proportions.

## Case reports

### *Case 1*

A 26-year-old woman had a history of psychosocial problems that included estrangement from her parents as well as anorexia nervosa and bulimia. In March 1984 she had started taking dimenhydrinate (Gravol) tablets daily for the drug's anorexic and sedative effects. To maintain these effects she progressively increased the dosage during the first 6 months, until she was taking 2500 mg/d. At these high levels the drug induced vomiting, which she later confided was a desirable effect; however, this side effect did not persist with continued abuse. Her friends found that she was confused and inattentive. She had difficulty socializing and could not keep a steady job as a secretary. Her abuse of the drug was corroborated by her boyfriend and a girlfriend, as well as by several pharmacists, who stopped her from continuing to purchase the drug in their stores after she had bought several large batches of tablets.

The patient's intake was regular for 15 months, until she was admitted to hospital for 12 days. During her hospital stay she did not take dimenhydrinate; she showed increased excitability and sympathetic activity and had an increased pulse rate, slightly elevated blood pressure and mydriasis. She reported extreme malaise. After discharge she returned to her previous intake of the drug.

A change in the patient's personal life 5 months later prompted her to seek medical help to stop her drug abuse. Her intake was gradually decreased from 1700 mg/d by one 50-mg tablet each day. No neurologic abnormalities were found at weekly follow-up visits.

The patient has not taken dimenhydrinate for 3 months; however, because of anxiety she took about 25 50-mg tablets a day on four occasions, the side effects each time being sedation and loss of appetite.

### *Case 2*

In 1981 a 25-year-old woman had taken dimenhydrinate tablets for a bout of severe vertigo of unknown cause. She continued to take the drug and increased the daily dose to between 500 and 600 mg. She liked the sedative effects, which were dose related.

Occasional vomiting occurred, and transient urinary retention developed that was thought to be secondary to the use of dimenhydrinate. The patient maintained the high daily dose but reduced it to 150 mg after 2 years. She found it difficult to think clearly but felt unwell each time she stopped taking the drug. Her intake was gradually stopped,

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but since then she has taken the drug on a few occasions.

In November 1985 the patient had a musculoskeletal complaint that was treated with nonsteroidal anti-inflammatory drugs and pethidine hydrochloride. As with dimenhydrinate, she became dependent on the pethidine.

## Comments

Dimenhydrinate is an ethanolamine-type antihistamine that blocks $H_1$ receptors.[1] It is used mainly to prevent motion sickness and to treat nausea. In short-term use sedation is the main side effect on the central nervous system (CNS); it is probably a result of the drug's antihistamine action. Histamine, produced in the posterior hypothalamus, inhibits the release of serotonin from the raphe neurons in the rostral brain stem.[2] The serotonergic system is considered to be important for the modulation of sleep.[3]

Although the drug is an antinauseant, it can be an emetic at high doses.[1] A massive overdose can cause marked CNS depression and seizures.[1] The lethal dose in children is reported to be 600 to 1000 mg. Anticholinergic effects, such as dilation and fixation of the pupils, can be mistaken as signs of an overdose of a tricyclic antidepressant.[1]

Drug dependence can be affected by psychologic as well as physical factors. The patients we have reported showed psychologic dependence, with habituation and compulsive use of the drug. Mild physical dependence apparently developed in the first patient, because withdrawal symptoms occurred after the drug was stopped abruptly. Tolerance clearly developed in both cases: the first patient ultimately tolerated doses that would ordinarily produce coma; the second patient became tolerant to the autonomic side effects and, to a lesser extent, the sedative effects.

Although uncommon, abuse of antihistamines has been reported: tripelennamine has been injected intravenously alone[4] and in combination with paregoric[5] or pentazocine;[6] diphenhydramine hydrochloride has been used intravenously with butorphanol;[7] and cyclizine, an antihistamine of the piperazine family, has been taken intravenously in combination with buprenorphine.[8] Antihistamines may decrease some of the unpleasant side effects of the other drug used in some combinations.[6]

Because of the availability, the low cost, and the sedative, anorexic and emetic properties of dimenhydrinate, abuse of this drug may be more common than is realized, especially among young women with anorexia or bulimia and among people with a history of drug dependence.

## References


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**Prove it**

*When Galen and Aristotle are unanimous in the expression of an opinion there lies absolute truth, but when they are at variance it is hard to decide, and we should arrive at the proper course of conduct by ratiocination. The skilled and experienced physician will act upon the promptings of his judgement.*

*— Rhazes (850-923)*